Remarks

Claims 1-25, 27-32, 34-36 and 61 are presently pending in the subject application. Reconsideration and allowance in view of the above amendments and the following remarks are respectfully requested.

The specification has been amended herein to address the Examiner's objections to the specification, as explained below, to update application information, and to correct an obvious error at page 4, lines 14-16, where Applicant mistakenly indicated that polynucleotide probes of the present invention have a net "positive" charge as opposed to a net "negative" charge. This error is clear from the specification, where it is taught, *inter alia*, that the probes of the present invention are negatively charged (*see* specification at paragraph bridging pages 29 and 30) and may consist entirely of DNA or RNA (*see* specification at page 4, lines 16-19). *See* MPEP § 2163.07.II at 2100-177 (8th ed., Rev. Feb. 2003) ("An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction. *In re Oda*, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971).

Claim 33 has been canceled herein without prejudice, and claim 34 has been amended herein to change the dependency from claim 33 to claim 1 and to delete redundant language.

Claim 1 has been amended herein to indicate that following: (i) the polynucleotide probe is negatively charged (*see, e.g.*, specification at paragraph bridging pages 29 and 30); (ii) the synthetic polycationic polymer is water soluble (*see, e.g.*, specification at page 6, lines 21-22); (iii) the sample is exposed to the dissociating reagent after the probe and the polymer have had sufficient time to associate in the sample and in an amount sufficient to dissociate the polymer from a probe:target duplex which may have formed in the sample (*see, e.g.*, specification at page 7, lines 5-11, and original claim 26); and (iv) the presence or absence of the probe:target duplex in the sample is determined as an indication of the presence or absence of the target nucleic acid (*see, e.g.*, specification at page 4, lines 7-13, and page 13, lines 3-15).

Claim 61 is newly added and recites that the probe and the polymer are independently provided to the sample. *See, e.g.*, specification at page 6, lines 20-21.

Objections to the Specification

The Examiner objects that Applicant's use of the trademark "TRITON X-100" is not accompanied by the generic terminology associated with this mark. Accordingly, Applicant has amended the specification herein to indicate that the TRITON® X-100 detergent is octoxynol. However, since Applicant has properly acknowledged that the term "TRITON X-100" is a trademark in the specification, it is unclear why the Examiner admonishes that "every effort [should be] made to prevent their use in any manner, which might adversely affect their validity as trademarks."

The Examiner further objects to Applicant's "catchall" statement incorporating by reference all documents referred to in the specification. In response, Applicant has amended the specification herein to incorporate only particular documents by reference.

Based on Applicant's amendments to the specification herein, withdrawal of the Examiner's objections to the specification are respectfully requested.

Rejections Under 35 U.S.C. § 112

Claims 1-36 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. (Applicant notes for this and subsequent rejections that claim 26 was previously canceled in a Response dated September 2, 2003.) Applicant respectfully traverses this rejection for the reasons that follow.

The Examiner states that the phrase "forming a duplex" encompasses the formation of both duplex and triplex structures, but fails explain why this interpretation of the claim language raises a written description issue. Applicant notes that the claims merely require conditions permitting the formation of a probe:target duplex and should not have to be supported by a written description regarding the formation of triplexes using the claimed polycationic polymers.

The Examiner further submits that the phrase "polycationic polymer" encompasses both organic and inorganic polycationic polymers, exhibiting a range of hydrophobicity and hydrophilicity, and can have virtually any upper mass. This, however, is not evidence or reasoning that Applicant has failed to adequately describe the claimed invention. Moreover, the specification goes to great lengths to describe the features of polycationic polymers that can be used in the claimed method. *See, e.g.,* specification page 27, line 24 *et seq.* Also, Applicant has amended the claims herein to indicate that the polycationic polymer is water soluble. *See, e.g.,* specification at page 6, lines 21-22. Therefore, if this rejection is to be maintained, then evidence or reasoning in support thereof is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner submits that the clause "in an amount sufficient to increase the association rate of said probe an [*sic*, and] said target nucleic acid" encompasses "values that both allow for an [*sic*, and] exceed this increased rate of association." As stated, Applicant is unable to determine what the basis is for the Examiner's rejection. The claims specify that the presence of the polycationic polymer in the sample increases the rate at which the polynucleotide probe and the target nucleic acid associate. If the claims require an increased rate of association, as they do, then it is unclear how the claim can be interpreted to also cover values which "exceed this increased rate of association." Put another way, if the claim specifies an increased rate of association, then there is no value that could exceed this increased rate of association since no upper limit is specified.

The Examiner argues that the phrase "preferentially hybridize" can be interpreted to encompass the formation of duplex structures with non-target sequences in nearly equal amounts. Applicant submits that the Examiner's interpretation is directly contradicted by the definitions section of the application, where the phrase "preferentially hybridize" is defined to mean "that under the specified hybridization assay conditions, polynucleotide probes can hybridize to their target nucleic acids to form stable probe:target hybrids indicating the presence of a specific target nucleic

acid sequence, and there is not formed a sufficient number of stable probe:non-target hybrids to indicate the presence of non-target nucleic acids." *See* specification at page 13, lines 3-15.

The Examiner urges that the dissociating reagent of claim 1 may be present in any amount, at any or all steps of the claimed method, and need not be present in an amount sufficient to cause any dissociation. In response, Applicant has amended claim 1 to specify that the sample is exposed to the dissociating reagent after contacting the probe and the target nucleic acid with the polymer, and to indicate that the dissociating reagent is provided in an amount sufficient to dissociate the probe from the polymer. *See, e.g.*, specification at page 5, lines 7-11.

The Examiner also observes that the claimed method encompasses the formation of a duplex structure between a wide variety of probes and target nucleic acids. Applicant first notes that what is claimed is not a novel probe, but rather a novel method for increasing the association rate between a polynucleotide probe and a target nucleic acid. Second, consistent with Applicant's theories of operation, any negatively charged polynucleotide probe of the present invention should be affected by the presence of the polycationic polymer, regardless of the probe's length or sequence. If, in light of this disclosure, the Examiner continues to doubt the adequacy of Applicant's written description, then Applicant respectfully requests that the Examiner provide evidence or reasoning to support such a position. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner notes that only six different polymers were tested in the examples. Given the nature of the claimed invention, the Examiner has not provided any reasoning or evidence why this is deemed an insufficient number of polycationic polymers to adequately describe the invention. Accordingly, such evidence or reasoning is specifically requested if the Examiner intends to maintain this rejection. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner further points out that only two probes, one target sequence and constant probe and target concentrations were tested under two sets of hybridization conditions. Again, the novelty of the invention does not lie in the particular probe or target nucleic acid selected, provided the probe is negatively charged. Moreover, the hybridization conditions employed in the examples are considered by Applicant to be more than adequate and were used simply to establish the rate enhancing effect of the polycationic polymers in both a low salt and a high salt set of hybridization conditions at two different tempartures. Thus, if the Examiner continues to question the adequacy of Applicant's disclosure, then evidence or reasoning to support the Examiner's determination is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

With respect to claims 28 and 30, the Examiner observes that there is no upper limit on the concentration of monovalent cations and contends that the specification does not provide an adequate written description of all concentrations of monovalent cations covered by the claims. In response, Applicant's note that the specification establishes that the invention works under both low and high salt concentrations, and that the claimed conditions permitting preferential hybridization of the probe to the target nucleic acid places an inherent upper limitation on the concentration of monovalent cations, depending on the nature of the probe and the target nucleic acid. Thus, if the Examiner wishes to maintain this rejection, then evidence or reasoning to support the Examiner's rejection is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner also notes that claims 28 and 30 have no upper temperature limit and contends that Applicant has failed to show that the claimed method can be practiced at any temperature above 40°C. Applicant respectfully directs the Examiner's attention to the examples section, where polycationic polymers were tested under hybridization conditions which included a reaction temperature of either 40°C or 60°C. Accordingly, if the Examiner still believes that these claims are not adequately supported by the written description, then supporting evidence or reasoning is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner additionally states that the "specification has not been found to set forth a reproducible procedure whereby unknown, yet highly complementary sequences would be prohibited from binding to probes." Applicant is uncertain why this rejection is being cast as a written description rejection. Nevertheless, Applicant submits that it is well known in the art of nucleic acid testing how to design and use probes having specificity for a particular target sequence. Furthermore, the specification has an entire section dedicated to hybridization conditions and probe design which would aid those skilled in the art in the design of target specific probes. *See* specification at page 19, lines 29 *et seq*. And, finally, Applicant has identified and incorporated by reference a number of documents which disclose methods for designing probes having specificity for a target nucleic in a test sample. *See, e.g.*, specification at page 6, lines 1-9, and page 21, lines 6-11. Thus, if the Examiner intends to maintain this rejection, then Applicant respectfully requests an explanation why this is a written description issue and, additionally, evidence or reasoning in support of this rejection. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

The Examiner also contends that Applicant's exemplification of only one label type does not support a range of possible labels for use with the claimed probes. (Applicant notes that a claimed embodiment does not have to be supported by examples in the specification in order to be adequately described.) A number of different labels are identified by Applicant in the specification. *See, e.g.*, specification at paragraph bridging pages 4 and 5; page 16, lines 19-30; and page 27, lines 3-22. Applicant submits that those skilled in the art would readily recognize how to use and detect these different types of labels in the claimed method without further description, and the Examiner has not provided any evidence or reasoning to suggest otherwise. Therefore, should the Examiner maintaining this rejection, then evidence or reasoning to support this rejection is respectfully requested. *See* MPEP § 2163.04 at 2100-173 (8th ed., Rev. Feb. 2003).

Based on the foregoing, Applicant submits that the claimed invention is supported by an adequate written description. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1-36 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as being non-enabled. The reasons for this rejection are the same as those set forth in the Examiner's written description rejection of claims 1-36. For the reasons presented above, Applicant submits that the claimed invention is supported by an adequate written description and is fully enabled. Accordingly, withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 101

Claims 1-36 stand rejected by the Examiner on the ground that the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. To support this rejection, the Examiner argues that: (i) the method promotes hybridization and dissociation of that which has hybridized; (ii) there is no requirement that the hybridization product be detected; and (iii) the claims encompass hybridizing random probes to unknown sequences. First, Applicant notes that the specification clearly discloses that dissociating the polycationic polymers from the polynucleotides can facilitate detection in some detection systems. *See, e.g.*, specification at page 7, lines 5-11, and page 37, lines 14-26. Second, there may be no hybridization product to detect because there may be no target nucleic acid in the sample being assayed, thus there was no claim requirement that the probe actually hybridize to the target nucleic acid. Third, the claimed invention does not contemplate random probes hybridizing to unknown sequences, as suggested by the Examiner, since the claims specifically recite that conditions are such that the probe will *preferentially hybridize* to the target sequence. *See, e.g.*, specification at page 13, lines 3-15. Moreover, Applicant notes that while the claims must be supported by a specific and substantial utility, there is no requirement that the claims must actually recite that utility. *See* MPEP § 2107 at

2100-29 (8th ed, Rev. Feb. 2003). And such a utility has been clearly identified by Applicant in the specification. *See, e.g.*, specification at page 3, line 1 *et seq.* Notwithstanding the foregoing, Applicant has amended the claims herein to recite the steps of a nucleic acid detection method. Accordingly, withdrawal of the Examiner's rejection is hereby respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1-36 stand rejected by the Examiner under 35 U.S.C. § 112, first paragraph, for allegedly not providing either a specific and substantial asserted utility or a well established utility for the reasons set forth in the Examiner's rejection under 35 U.S.C. § 101. For the reasons set forth above, Applicant submits that the grounds for this rejection are improper and, moreover, have been rendered moot by the amendments to the claims herein. Accordingly, Applicant hereby respectfully requests withdrawal of this rejection.

The Examiner notes that claims 33-36 require the performance of a determination step, but contends that the claims are not enabled because there is no requirement that unbound probe be separated from probe which has bound to the target sequence, nor, according to the Examiner, is there any disclosed procedure for distinguishing the signal of probe bound to the target nucleic acid from the signal of probe bound to "non-target entities." First, Applicant notes that the specification clearly discloses the use of homogenous assays that do not require that bound probe be separated from unbound probe in order to detect the targeted duplex. *See, e.g.*, specification at page 36, line 12 *et seq.* Moreover, the Examiner's contention that the specification does not disclose how to distinguish probe bound to target from probe bound to non-target ignores the claim limitation that the probe *preferentially hybridize* to the target nucleic acid under the conditions of the method. *See, e.g.*, specification at page 13, lines 3-15. Thus, Applicant submits that the claimed invention is fully enabled. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1-7 and 10-36 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,255,476 to Vinayak *et al.* Applicant traverses this rejection on the ground that no teaching has been identified that would motivate those skilled in the art to expose the sample to a dissociating reagent in an amount sufficient to dissociate the polymer from the duplex after the probe and the target nucleic acid have had sufficient time to associate in the sample, as claimed. Accordingly, withdrawal of this rejection is respectfully requested.

Claim 8 stands rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Vinayak *et al.* as applied to claims 1-7 above, and further in view of U.S. Patent No. 6,380,377 to Dattagupta. Applicant submits that the noted deficiencies of Vinayak are not addressed by Dattagupta. Accordingly, withdrawal of this rejection is respectfully requested.

Applicant notes for the record that the Examiner cites a portion of U.S. Patent No. 5,731,148 to Becker *et al.* as being pertinent to Applicant's disclosure, but does not expound on the purported relevance of this reference to the subject application, especially the pending claims.

Certificate of Transmission

I hereby certify that this correspondence (and any referred to as attached) is being sent by facsimile to 703-872-9306 on the date indicated below to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Respectfully submitted,

Date: August 26, 2004

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